REMARKS

Reconsideration and withdrawal of the requirement for restriction are respectfully requested in view of the remarks herewith.

The Office Action required restriction under 35 U.S.C. §121 from among one of the following groups of inventions:

Group I: Claims 1, 3-17, 20, 21, 28-32, 45-69, 93 drawn to a reverse genetics system for screening and identifying antiflaviviral compounds, a recombinant plasmid, a cell line, a DNA molecule, classified in class 424, subclass 184.1;

Group II: Claims 2-17, 20, 21, 28-32, 45-69, 93 drawn to a reverse genetics system for screening and identifying attenuated flaviviral vaccines, a recombinant plasmid, a DNA molecule, a cell line, classified in class 424, subclass 184.1;

Group III: Claim 18, drawn to a method for preparing a fully infectious RNA transcript, classified in class 536, subclass 23.1;

Group IV: Claims 19, 22-27, drawn to a method for preparing a cell line, classified in class 435, subclass 325;

Group V: Claims 33, 39, 70-92 drawn to a method of identifying potential antiflaviviral chemotherapeutics, a high throughput assay for screening and a method for screening a plurality of compounds, and a composition, classified in class 424, subclass 184.1;

Group VI: Claims 34-38, drawn to a method of collecting and transmitting a dataset, classified in class 710, subclass 717;

Group VII: Claim 40, drawn to a method for administering the pharmaceutical composition, classified in class 424, subclass 184.1;

Group VIII: Claims 41, 42, drawn to a method for generating a potential attenuated WNV vaccine, classified in class 424, subclass 184.1;

Group IX: Claim 43, drawn to a method of generating a live attenuated WNV lineage I virus vaccine, classified in class 424, subclass 184.1; and

Group X: Claim 44, drawn to a method of treating a flaviviral infection, classified in class 424, subclass 184.1.

Further, in the event that election of Group I is made, the Restriction Requirement states that an election of species is required since the claims of Group I allegedly recite products that have distinct functions, distinct structures, and distinct physical, chemical and functional properties. Thus, the Restriction Requirement requires an election of:

(a) either a cDNA clone (as in claim 3) or a lineage I WNV replicon (as in claim 4);

(b) one reporter (as in claims 7 or 47);

(c) one promoter (as in claim 13) and if a viral promoter is elected, then one kind of viral promoter (as in claims 14 or 54); and

(d) one structural gene (as in claim 50).

In the event that a Group II election is made, the Restriction Requirement requires an election of species as follows:

(a) either a cDNA clone (as in claim 3) or a lineage I WNV replicon (as in claim 4);

(b) one reporter (as in claims 7 or 47);

(c) one promoter (as in claim 13) and if a viral promoter is elected, then one kind of viral promoter (as in claims 14 or 54); and

(d) one structural gene (as in claim 50).

In the event that election of Group IV is made, an election of one of the flaviviruses of claim 23 is required.

Should an election of Group V be made, the Restriction Requirement further requires an election of one of the cell types of claim 74, one of the reporters of claim 77, one of the cell types of claim 85, one of the reporters of claim 88, one of the flaviviruses of claim 89, and one of the flaviviruses of claim 90.

Group I, claims 1, 3-17, 20, 21, 28-32, 45-69, 93 drawn to a reverse genetics system for screening and identifying antiflaviviral compounds, a recombinant plasmid, a cell line, a DNA molecule, classified in class 424, subclass 184.1, is hereby provisionally elected, with traverse, for further prosecution in this application. Further, as a provisional election of Group I is made, the following further species elections are made:

(a) a lineage I WNV replicon (as in claim 4);

(b) a green fluorescent protein reporter (as in claim 7);

(c) a T7 promoter (as in claim 14) and

(d) an envelope gene (as in claim 50).

Applicants reserve the right to file divisional applications to non-elected subject matter. Reconsideration and withdrawal of the requirement for restriction and the requirement for election of species are respectfully requested in view of the remarks herewith.

Applicants further request a modification of the Restriction Requirement such that Group I claims are rejoined with, and thus searched and examined together with, the claims of Groups II, V, VII, VIII, IX and X since the claims of these Groups share the identical search classification. Further, Applicants additionally request further modification of the Restriction Requirement such that the claims of Group I are further rejoined with the claims of Groups III, IV, V, VI, VII, VIII, IX and X since the method claims in those Groups depend from and/or include the limitations of the reverse genetics system of Group I. Accordingly, Applicants respectfully submit that no serious burden would be placed on the Examiner to search and examine the claims of Groups I, II, III, VI, V, VI, VII, VIII, IX and X. And, it is especially requested that Groups I, II and V be examined together, or at the minimum Groups I and V, for the herein reasons.

As a traverse, it is noted that the MPEP lists two criteria for a proper restriction requirement. First, the inventions must be independent or distinct. MPEP § 803. Second, the examiner must examine the entire application on the merits **"[i]f the search and examination of an entire application can be made without serious burden, ...even though it includes claims to distinct or independent inventions."** *Id.* Accordingly, the MPEP directs the examiner to search and examine an entire application regardless of whether it includes distinct or independent inventions where no serious burden is placed on the examiner by the search and/or examination.

Many of the Groups, as noted above, are commonly classified under class 424, subclass 184.1. This includes most of the Groups of claims, namely, Group I, II, V, VII, VIII, IX and X. The fact that these sets of Groups are identically classified necessarily indicates that search and examination of at least those claims commonly classified would be coextensive and thus, there would not be an undue burden placed on the Examiner. Therefore, it is respectfully submitted that at least a subset of the Groups that are commonly classified should be subject to rejoinder, for example, Groups I, II and V or Group I together with Group V.

Moreover, all of the claims taken together as originally filed and presented herein represent a web of knowledge and continuity of effort that merits search and examination as a

single invention. The invention as disclosed in the present application relates broadly to a novel reverse genetics system, and methods for making and using the reverse genetics system, especially a lineage I WNV cDNA or replicon system, which can be used to screen for novel antiflaviviral chemotherapeutics or vaccines that are effective to treat or immunize against flavivirus infections, such as, WNV. The claims of the invention all require, relate or involve the reverse genetics system and thus each claim is inextricably linked under the same inventive concept.

For example, the reverse genetics system can be introduced into a cell line (e.g., claim 21) or be used in a screening assay (e.g., claims 70 or 80). Further, the reverse genetics system may be used to identify potential antiflaviral chemotherapeutics (e.g., claim 33) and to generate attenuated WNV vaccines (e.g., claims 41 and 43). An embodiment of the reverse genetics system includes a DNA molecule encoding a mRNA of lineage I WNV genome (e.g., claim 45). Accordingly, it is respectfully asserted that each of the claims of the present application fall within the same inventive concept and thus, search and examination of the entire application would not be unduly burdensome on the part of the Examiner.

Further, in view of the requirement for an election of species, whereby the Examiner requires an election of one reporter (e.g. claim 7), one promoter (e.g. claim 13), and one structural gene (e.g. claim 50) from Markush groups, the Examiner is respectfully requested to review M.P.E.P. § 803.02 which states "[i]f the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions." Furthermore, in view of M.P.E.P. § 803, when the generic claim includes sufficiently few species that a search and examination of all the species at one time would not impose a serious burden on the examiner, then a requirement for election is inappropriate.

In the instant case, there is a disclosure of relationship between the claimed species of reporters, promoters and structural genes. Applicants' Group I claims are generally directed to a reverse genetics system for screening and identifying antiflaviviral compounds. The reverse genetics system can be a lineage I WNV replicon and can comprise a promoter sequence operably linked to the WNV replicon and a first nucleotide sequence that encodes a reporter. The specification discloses that "the expression of the reporter-encoding nucleotide sequences

can be monitored and/or measured to indicate the replication activity of WNV RNA." See page of the as-filed application. In addition, the specification states that the reverse genetics system can be operably linked to a promoter to provide for in vitro transcription. Consequently, there is a disclosed relationship between the species of reporters as they can be used to monitor and/or measure WNV RNA replication activity. Further, the claimed species of promoters are related as they can be used to control in vitro transcription of the reverse genetics system. The Group I claims further are directed to a DNA molecule having a DNA sequence encoding a mRNA of a lineage I WNV genome having a deletion in one or more structural genes of the lineage I WNV genome. The Markush group of claim 50 includes only three species of structural genes, the capsid, envelope and membrane genes. This Markush grouping contains species which are both "sufficiently few in number" and are "closely related" by virtue of the fact that they represent the only known structural genes of WNV.

Additionally, the claims are not broken into separate classifications on the basis of which species is claimed. Consequently, it can be assumed that the classification of all the claims into a single group was made considering each of the species, such that the search of any species would be co-extensive and include the remaining species.

Accordingly, search and examination of all claimed species of promoters, reporters and structural genes would not place any undue burden on the Office and, respectfully, the requirement for election of species should reconsidered and withdrawn.

Specific comments as to the individual asserted grounds for restriction presented in the Office Action are as follows.

The assertion in the Office Action that the claims of Group I are distinct from those claims of Groups II on the grounds that they "identify separate products having distinct functions, distinct structures, and distinct physical, chemical and functional properties" is misguided. As noted above, the claims of Group I and II are both classified under the same class (424) and subclass (184.1) and therefore search and examination of Group I claims would necessarily be coextensive with and would encompass the claims of Group II. Moreover, since the claims of Group I and Group II all relate to the reverse genetics system of the invention, it does not seem logical that Groups I should be restricted from the claims of Group I. Accordingly, as the claims of Groups I and II are overlapping under a unified inventive concept, search and examination of Group I claims would necessarily encompass Groups II. Therefore, it

is respectfully submitted that search and examination of both Groups together would not impose a serious burden on the Examiner.

The Office Action states that the claims of Groups III, IV, V, VI, VII, VIII, IX and X are unrelated and have different functions, effects and modes of operation. It is respectfully submitted that any search of the claims of Group I would certainly encompass references for the subject matter of the claims of Groups III, IV, V, VI, VII, VIII, IX and X as most of the Groups have identical classification (i.e. class 424, subclass 184.1). Moreover, each of the Groups overlaps with the unified inventive concept of the invention, namely the novel reverse genetics system of the invention. Indeed, the reverse genetics system of the invention can be introduced into a cell line and used to identify potential antiflaviviral chemotherapeutics (e.g., see claims of Groups III and V). Therefore, it is respectfully submitted that search and examination of the claims of Group I together the Groups III, IV, V, VI, VII, VIII, IX and X claims would not place an undue burden on the Examiner.

The Restriction Requirement contends that the claims of Groups I, II and Groups III, VIII and IX are related as product and process of use. In addition, the Examiner states that Groups I, II and IV are related by product and process of use. The Restriction Requirement further indicates that Groups V is related by product and process of use to Groups VII and X. It is respectfully asserted, however, that any search for the subject matter of the claims of Group I would certainly encompass references relevant to the claims of Groups II, III, IV, V, VII, VIII, IX and X. First, most of the claims of the Groups are classified under the identical class and subclass of inventions and thus, necessarily a search of either set of claims would encompass the other. Further, as the claims of both Group I and the claims of Groups II, III, IV, V, VII, VIII, IX and X involve a stably replicating reverse genetics system of the invention, search of Group I claims would certainly encompass the claims of the other Groups. In other words, the claims of Group I are unified with the claims of Groups II, III, IV, V, VII, VIII, IX and X under the umbrella of the same inventive concept, i.e. the reverse genetics system of the invention. Therefore, Applicants respectfully submit that it would not impose any serious burden on the Examiner to search and examine Groups I, II, III, IV, V, VII, VIII, IX and X simultaneously as most of the claims have identical classification and all overlap in subject matter with the claims of Group I with respect to the reverse genetics system of the invention.

In view of the remarks herein, enforcing the present Restriction Requirement would result in inefficiencies and unnecessary expenditures by the Applicants and the PTO, as well as extreme prejudice to Applicants (particularly in view of GATT, whereby a shortened patent term may result in any divisional applications filed). Restriction has not been shown to be proper, especially in view of the requisite showing that a serious burden has not been met. Indeed, the search and examination of each commonly classified Group would likely be co-extensive and, in any event, would involve such interrelated art that search and examination of the entire application can be made without undue burden on the Examiner. All of the preceding, therefore, mitigate against restriction.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal, or at least modification, of the Restriction Requirement, such that, at the least or at least a portion thereof of the claims of Groups I, II, III, VI, V, VI, VII, VIII, IX and X are examined together. And, it is especially requested that Groups I, II and V be examined together, or at the minimum Groups I and V, for the herein reasons.

CONCLUSION

Reconsideration and withdrawal, or modification of the restriction requirement, and a prompt and favorable examination on the merits, is respectfully requested.

Respectfully submitted,
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